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Society for Cardiovascular Angiography and Interventions 2010 and EuroPCR 2010

An Update in Interventional Cardiology

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Several breaking trials in the field of interventional cardiology were presented at the 33rd annual scientific session of the Society for Cardiovascular Angiography and Interventions (SCAI) held in San Diego, California, May 5 to 8, 2010, and at EuroPCR 2010, held in Paris, France, May 25 to 28, 2010. A brief overview of key results is presented here.

2-Year Interim Results of the Zilver Peripheral Paclitaxel-Eluting Stent (PES)

This single-arm registry (completed outside the U.S.) included 787 patients with symptomatic disease of femoropopliteal arteries with a reference vessel diameter of 4 to 9 mm treated with the Zilver polymer-free peripheral arterial PES (Cook Medical, Bloomington, Indiana) (1). A total of 900 lesions were treated: with a mean lesion length of 100 ± 82 mm, 38% total occlusions, and 28% restenotic lesions; on average, 1.9 stents were used per lesion. The primary end points were safety (event-free survival and freedom from procedure- or device-related mortality or amputation), stent integrity (freedom from device-related morbidity or complications), and effectiveness (freedom from clinically driven target lesion revascularization [TLR]). At 2-year follow-up, which was completed for 451 patients, event-free survival was 80%, with no device-related deaths, but with 4 procedure-related deaths (0.9%) and 1 amputation (0.2%). In 2 years, 81 patients (18%) underwent clinically driven TLR, and 2 patients (0.4%) had a worsening Rutherford classification. Of the total 1,432 stents implanted in the study (maximum of 4 stents/patient), there were 22 fractures (1.5%), of which 14 caused displacement of segments of the stent.

Although these interim results sound promising for a drug-eluting stent in the peripheral vasculature, confirmation will arrive only with future randomized studies with longer follow-up. The inherent limitations of this single-arm study (no control group) will be addressed in the ongoing, 480-patient randomized controlled trial comparing the same peripheral arterial PES to balloon angioplasty followed up to 5 years. Although approved in Europe, the Zilver PES is still awaiting approval by the Federal Drug Administration (FDA) in the U.S.

The EVEREST II Update

The EVEREST II (Endovascular Valve Edge-to-Edge REpair STudy II) (2) randomized 2:1 a total of 279 patients with moderate to severe (3+) or severe (4+) mitral regurgitation (MR) (3) to either percutaneous mitral valve repair (n = 184) with the MitraClip device (Abbott, Abbott Park, Illinois) or surgical repair/replacement (n = 95). Primary end points of the study were major adverse events at 30 days and clinical success rate, defined as freedom from a combination of death, mitral valve surgery or reoperation for mitral valve dysfunction, and MR grade >2+ at 12 months. Preliminary 2-year Kaplan-Meier estimates of freedom of reoperation (in the control arm) or first mitral valve operation (in the device arm) on an intention-to-treat basis were approximately 96% and just under 80%, respectively. In addition, results of device-treated

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patients were presented according to MR etiology (degenerative [n = 135] or functional [n = 49]). Patients with functional MR significantly more often had coronary artery disease and prior coronary artery bypass surgery compared with patients with degenerative MR. The 30-day modified major adverse event rates were comparable for patients with degenerative (8.1%) and functional (8.2%) MR; reduction of MR severity to 1+/2+ at 12-month follow-up was similar for degenerative (82.8%) and functional (78.1%) MR patients; and the improvement in New York Heart Association functional classification to I/II at 12 months was equal in degenerative (97.8%) and functional (96.7%) MR patients.

The favorable results of this study offer the MitraClip procedure as a reasonable percutaneous option for selected patients with significant mitral regurgitation compared with surgery. However, the device is awaiting approval in the U.S. by the FDA, and although already approved in Europe, will require a learning curve by operators prior to replicating these results.

The RESOLUTE III Trial

The RESOLUTE III trial (4) was a large-scale comparison of 2 drug-eluting stents powered to detect noninferiority in the primary end point of target lesion failure (TLF) (defined as cardiac death, myocardial infarction attributable to the target vessel, and clinically driven TLR). A total of 2,300 patients were randomized in this all-comer trial to treatment with the Endeavor Resolute zotarolimus-eluting stent (ZES) (Medtronic, Santa Rosa, California) (n = 1,150) or the Xience V everolimus-eluting stent (EES) (Abbott Vascular, Santa Clara, California) (n = 1,150). The Resolute ZES has the same cobalt chromium stent platform and drug as the previous Endeavor ZES but features a different polymer, allowing for a longer duration of drug release due to its novel topcoat. Baseline characteristics were well matched, but the EES group had a higher number of stents used per patient (2.0 ± 1.3 vs. 1.9 ± 1.2, p = 0.02) and a longer stent length per patient (37.0 ± 26.5 mm vs. 34.4 ± 24.5 mm, p = 0.02). The 12-month TLF rates were 8.2% in the ZES group and 8.3% in the EES group (p for noninferiority <0.01). Cardiac death (1.3% vs. 1.7%, p = 0.61), target vessel myocardial infarction (4.2% vs. 4.1%, p = 0.92), and clinically driven TLR (3.9% vs. 3.4%, p = 0.50) were similar for patients treated with ZES and EES. Of note, the 12-month rate of definite stent thrombosis was significantly higher in the ZES arm (1.2% vs. 0.3%, p = 0.01).

Although the increased rates of definite stent thrombosis in the ZES arm despite the use of higher number and longer length of stents per patient in the EES arm could be a cause for concern, the study was only powered for the primary end point, and definitive conclusions will require longer follow-up in large trials that have sufficient statistical power to detect differences in rates of stent thrombosis.

The NEVO RES-ELUTION I Trial

The NEVO RES-ELUTION I trial (5) enrolled a total of 394 patients with single de novo native coronary artery lesions randomized to treatment with the Nevo sirolimus-eluting stent (SES) (Cordis, Miami Lakes, Florida) or the Taxus Liberté PES (Boston Scientific, Natick, Massachusetts). The Nevo SES features a cobalt chromium stent platform with a biodegradable polymer that elutes sirolimus from reservoirs on the abluminal surface of the stent. The primary end point of in-stent late loss was significantly lower at 6 months with Nevo SES than with PES (0.13 ± 0.31 mm vs. 0.30 ± 0.46 mm, p < 0.01). Moreover, there was a weak trend towards lower major adverse cardiac events (defined as death, myocardial infarction, or TLR) in the Nevo SES compared with the PES group (6.1% vs. 10.8%, p = 0.14) at 12-month follow-up. No cases of stent thrombosis occurred in the Nevo SES group; 1 probable and 1 possible stent thrombosis occurred in the PES group up to 12-month follow-up.

The Nevo SES introduces a unique stent design with promising results. Although the trial was not powered for clinical end points, the results for the Nevo SES suggest that there are no differences in major adverse cardiac events between the 2 groups. Future comparisons against second-generation drug-eluting stents in larger groups of higher-risk patients remain to be seen.

The ABSORB Cohort B Trial

The second phase of the ABSORB (A Bioabsorbable Everolimus-Eluting Coronary Stent System for Patients With Single De-Novo Coronary Artery Lesions) trial (Cohort B) (6) enrolled 101 patients from 12 centers (outside the U.S.) treated with revision 1.1 of the everolimus-eluting bioabsorbable vascular scaffold (BVS, Abbott Vascular). Six-month results for the first 45 patients, with up to 2 de novo native coronary artery lesions <14 mm in length and a reference vessel diameter of 3.0 mm, were presented. The design of the BVS was modified to address the issue of nonsignificantly increased late recoil with the BVS revision 1.0 compared with the Xience V EES (Abbott Vascular) (7) and incorporated device enhancements designed to improve deliverability and vessel support. The revision 1.0 design of the BVS was absorbed within 2 years after implantation; although no long-term data on absorption of the revision 1.1 design are currently available, it is expected to have a similar absorption profile (6). In the first 45 patients of ABSORB Cohort B, in-stent late loss was 0.19 mm at 6-month angiographic follow-up. The 6-month major adverse cardiac event rate (defined as cardiac death, myocardial

infarction, or ischemia-driven TLR) was 4.4%. Furthermore, no stent thrombosis had occurred at 6 months.

The ABSORB trial has shown that the theoretical aims of the bioabsorbable stent are close to becoming a reality. Although this cohort implies safety of the new revision of BVS, the overall safety of these devices requires further confirmation in large future event-driven clinical trials.

The DEBIUT Trial

The DEBIUT (Drug-Eluting Balloon In Bifurcation Trial) investigators randomized 120 patients with coronary bifurcation lesions in a 1:1:1 ratio to provisional T-stenting and final kissing balloons with a paclitaxel-eluting balloon (PEB) (Dior balloon, Eurocor, Bonn, Germany) and bare-metal stent (BMS), standard balloon (STB) and PES, or STB and BMS (8). The primary end point of side-branch late lumen loss did not significantly differ between the 3 treatment groups (PEB+BMS: 0.04 mm, STB+DES: 0.11 mm, STB+BMS: 0.10 mm). At 6-month follow-up, there were no deaths, and only 1 patient had stent thrombosis, in the STB+PES arm. Although a numerical reduction in 6-month TLR was observed with the PEB+BMS (12.5%) and STB+PES (10.0%) arms compared with the STB+BMS arm (27.5%), this difference did not reach statistical significance.

Drug-eluting balloons offer a novel technique in attempts to curb restenosis in complex lesion subsets. Although this study did not reach statistical significance for reduction in TLR with PEB, the safety profile and 6-month clinical trends pave the way for larger randomized trials with longer follow-up for definitive conclusions.

Summary

The 2010 SCAI and EuroPCR scientific sessions presented some new data on breaking clinical trials and established follow-up data on some previously initiated trials in interventional cardiology, which have been summarized. Further details on these studies can be accessed at the American College of Cardiology's *Cardiosource* website (9).

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